

News and Views from the Literature

T1 Bladder Cancer

Selecting Patients for Immediate Cystectomy

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Management of high-grade urothelial carcinoma of the bladder involving the lamina propria (stage T1) but not penetrating into the muscularis propria represents a challenge for both physician and patient. There is no level I evidence to direct us. Transurethral resection (TUR) has long been recognized as an inadequate complete treatment, with recurrence rates approaching 80% and the risk of progression to muscle invasion approaching 60%.^{1,2} Adjuvant intravesical therapy with Bacille Calmette-Guérin (BCG) or chemotherapeutic agents, such as mitomycin C, may decrease the overall recurrence rate by approximately 30% compared with TUR alone,^{3,4} but tumor progression still occurs in 15% to 40% of patients within the first 5 years, and these patients are at risk of dying from urothelial cancer.^{4,5} It remains difficult

to accurately identify life-threatening, high-grade T1 tumors. Multiple tumors, larger size (more than 3 cm), carcinoma in situ (CIS), and tumor at first follow-up cystoscopy after treatment are associated with greater risk of disease progression and reduced survival. Other prognostic factors under investigation are lymphovascular invasion, depth of lamina propria invasion, and tumor marker expression.⁶⁻⁸

Can Restaging Transurethral Resection of T1 Bladder Cancer Select Patients for Immediate Cystectomy?

Herr HW, Donat SM, Dalbagni G.

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This article by Herr and colleagues shows that restaging TUR can identify patients at high risk for tumor progression, and, thus, can be used to stratify which patients should be offered early cystectomy. A cohort of 352 patients with T1 bladder cancer underwent a second or restaging TUR after a 2- to 4-week interval. All patients received induction BCG therapy, but none received maintenance therapy. Overall 203 (58%) had residual tumor on restaging TUR, from which 92 (26%) had T1 cancer. During the first 5 years, 66% of patients experienced disease recurrence, and 35% experienced progression to muscle-invasive disease. Five-year progression rates based on findings on restaging TUR increased from 8% for patients

with no residual tumor to 16% for those with residual TaG3 tumor, to 37% for those with CIS, and reached 82% for those with residual T1 tumor. In other words, 75 of the 92 patients with residual T1 cancer on restaging TUR (82%) experienced disease progression to muscle invasion within the first 5 years (median follow-up 7.5 years [range: 1-14]). In a multivariate analysis of risk factors, restaging TUR pathology was the most important single determinant associated with tumor progression (HR 6.7; $P < .001$) followed by the presence of complete response to BCG at first cystoscopy performed 3 to 6 months after TUR (HR 2.7; $P < .001$), presence of multiple tumors (HR 3.3; $P = .04$), and high-grade disease (HR 3.1; $P = .05$). These authors found that the majority of patients with high-grade T1 who had residual T1 cancer on restaging TUR had life-threatening muscle-invasive cancer within 12 to 17 months despite bladder-sparing methods. There was a clear difference in progression rates between T1 low-grade and high-grade categories. The authors concluded that patients who have high-grade T1 disease on restaging TUR at 2-4 weeks after primary resection are at high risk for early tumor progression and therefore should be considered for/offered early cystectomy.

This study has limitations. First and foremost, it is a retrospective study. Second, some of the patients may not have undergone complete TUR in the first instance. Third, none of the patients received maintenance BCG, an approach that has been demonstrated to decrease progression rates relative to induction BCG alone. Fourth, none of the patients had immediate postoperative chemotherapy to reduce post-resection seeding, a technique that has been confirmed in multiple, randomized, clinical trials and a meta-analysis to reduce tumor recurrence significantly.⁹ However, I believe that intravesical therapy targets “floating” cells and abnormal bladder mucosa not included in the resection sites, whereas TUR is directed at eradicating the invasive component of the disease. Therefore, incomplete resection and tumor implantation can be avoided by including biopsy adjacent to the tumor, extended resection of the base and margins, and immediate postoperative chemotherapy.

The evidence of a high incidence of residual or recurrent bladder tumor (64%-78%) following resection by competent, experienced urologists is consistent and convincing, and supports the routine use of repeat TUR.^{10,11} Therefore one should perform routinely a second TUR 2-6 weeks after the first to identify patients at high risk of early tumor recurrence and progression. This is preferable to waiting for progression to muscle-invasive disease, as high-risk patients who would benefit from immediate cystectomy can be identified in time. Herr and Donat’s earli-

er work suggested that these patients might be better served by immediate cystectomy rather than BCG therapy.

Understaging is among the limitations of effective surveillance and appropriate treatment. The accuracy of staging is poor, with only 50% of clinical T1 patients accurately staged.¹²⁻¹⁴ Several reports have shown that approximately 10%-15% of patients treated with radical cystectomy for high-grade T1 disease have lymph node metastases.¹⁵⁻¹⁸ The rate of nodal involvement increases proportionally to the number of TURs before cystectomy.¹⁵ Radical cystectomy is a highly effective treatment for pathologically organ-confined bladder cancers, with 5-year recurrence-free survival rates ranging from 80% to 88%.^{18,19} Patients with clinical stage T1 cancers who undergo early rather than delayed cystectomy have substantially better 5-year recurrence-free survival rates (90% vs 62%).²⁰ Moreover, patients who experience progression to muscle-invasive disease have a significantly worse survival compared with those who present with de novo clinical T2 disease (3-year bladder-cancer-specific survival: 37% vs 67%).²¹ Moreover, patients with high risk non-muscle-invasive bladder tumors who underwent earlier rather than delayed cystectomy for tumor relapse after initial treatment with TUR and BCG therapy were shown to have a better survival rate (92% for patients who underwent cystectomy less than 2 years after initial BCG therapy vs 56% for patients treated after 2 years).²² Taken together, these data imply that radical cystectomy should be performed sooner rather than later for recurrent high-grade T1 cancers. Therefore, with current limitations of staging modalities, waiting for muscle-invasion before performing cystectomy may be too late for optimal quality of life and oncologic outcomes in patients with high-grade T1 bladder cancer. Patients must be counseled and educated early regarding the need for cystectomy so that it does not come as a surprise and lead to unwanted delay. Despite technical advances that may minimize the impact of bladder removal on health-related quality of life, such as nerve-sparing and prostate-sparing techniques, and the application of orthotopic urinary diversion to a broad array of patients in certain centers, the functionality of diversion typically falls short of that of the native bladder. Furthermore, the perioperative consequences of radical cystectomy are not trivial, with morbidity and mortality rates approaching 30% and 3%, respectively.²⁰

Given the potential benefits and trade-offs associated with cystectomy for clinical stage T1 bladder cancer, in what contexts is extirpative treatment appropriate? The ideal candidate for conservative treatment of T1 bladder cancer is a patient with a solitary or at least completely resectable tumor, a negative upper-tract evaluation, and

no evidence of invasive disease in the prostatic urethra. Patients with T1 tumors should be considered for cystectomy if they have:

1. multifocal or extensive tumors that cannot be completely and reliably resected, either during the first resection or soon thereafter
2. deep penetration of the lamina propria approaching muscularis propria
3. involvement of the prostatic mucosa or ducts
4. recurrent T1 within 3 months after intravesical therapy
5. residual T1 disease on repeat TUR
6. concurrent CIS or onset while receiving therapy
7. micropapillary variant
8. extensive invasion of the lymphatic space
9. poor patient compliance

The presence of 1 or more of these risk factors should prompt the clinician to consider the pitfalls of proceeding with conservative treatment compared with the trade-offs of radical cystectomy. Whereas a single risk factor may not be sufficient to warrant early cystectomy, the aggregate risk of multiple factors supports the need for immediate cystectomy. ■

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Incontinence

Curing Stress Urinary Incontinence, or Shades of Dryness

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Historically the gold standard in treatment of stress urinary incontinence (SUI) in urologists' hands is the pubovaginal sling, whereas gynecologists have often preferred the Burch and MMK procedure. The age-adjusted rate of inpatient surgical procedures for SUI in women in the United States increased from 0.32 per 1000 women in 1979 to 0.60 per 1000 women in 1997. Given the aging of the US population, the total number of procedures for treatment of SUI is expected to continue to rise. Yet there are few data from randomized trials to inform surgical decision making. We would like to review an important recent paper and companion editorial on this topic in the *New England Journal of Medicine*.